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Run training ameliorates the established erectile dysfunction in rats under long-term nitric oxide (NO) blockade

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Introduction

Stimulation of nitrergic neurons and endothelial cells in the erectile tissue results in release of NO that diffuse to surrounding smooth muscle cells where it activates the soluble guanylate cyclase (sGC), facilitating the conversion of GTP to cGMP. This second messenger diminishes the intracellular levels of calcium thereby causing penile smooth muscle relaxation and penile erection [1]. Epidemiological studies have shown a strong association between erectile dysfunction (ED) and arterial hypertension [2], where the deficiency of the NO-cGMP pathway seems to greatly contribute to such association [3]. Regular physical exercise has been shown to increase the NO production thus ameliorating cardiovascular diseases [2,4]. Recently, we have shown that prior physical conditioning improves the erectile function in normotensive rats [5] and prevents the impaired corpus cavernosum relaxation secondary to chronic NO blockade in rats [2].

Propose

The aim of this work was to evaluate whether regular run training restores the established ED in made hypertensive by chronic treatment with the NO synthesis inhibitor L-NAME.

Methods

Wistar rats were divided into control sedentary (C-SD), control trained (C-TR), L-NAME sedentary (LN-SD) and L-NAME trained (LN-TR) groups. Rats were treated with L-NAME (10 mg/rat/day) or tap water alone for 8 weeks. The run training program initiated after 4 weeks of L-NAME treatment. It consisted in 4 weeks in a treadmill, 5 days/week, each session lasting 60 min. The nitregic relaxing responses were evaluated by both electrical field stimulation (EFS) of corpus cavernosum *in vitro* and measurement of intracavernosal pressure (ICP) in response to electrical stimulation of the cavernous nerve (*in vivo* experiments). The plasma levels of nitrite/nitrate (NOx) were also measured.

Results

Physical exercise reduced significantly the L-NAME-induced arterial hypertension (103 ± 4, 95 ± 3, 154 ± 7 and 120 ± 5 mmHg, mean arterial pressure for C-SD, C-TR, LN-SD and LN-TR groups, respectively; N = 8–12). The in vitro and in vivo nitrergic-dependent relaxing responses were significantly reduced in LN-SD group compared with C-SD, as expected. The run training program significantly restored the in vitro EFS-induced relaxing response (Figure 1a) and the in vivo erectile function (Figure 1b and 1c). Plasma NOx concentrations were significantly reduced in LN-SD (19 ± 3 μM) compared with C-SD (28

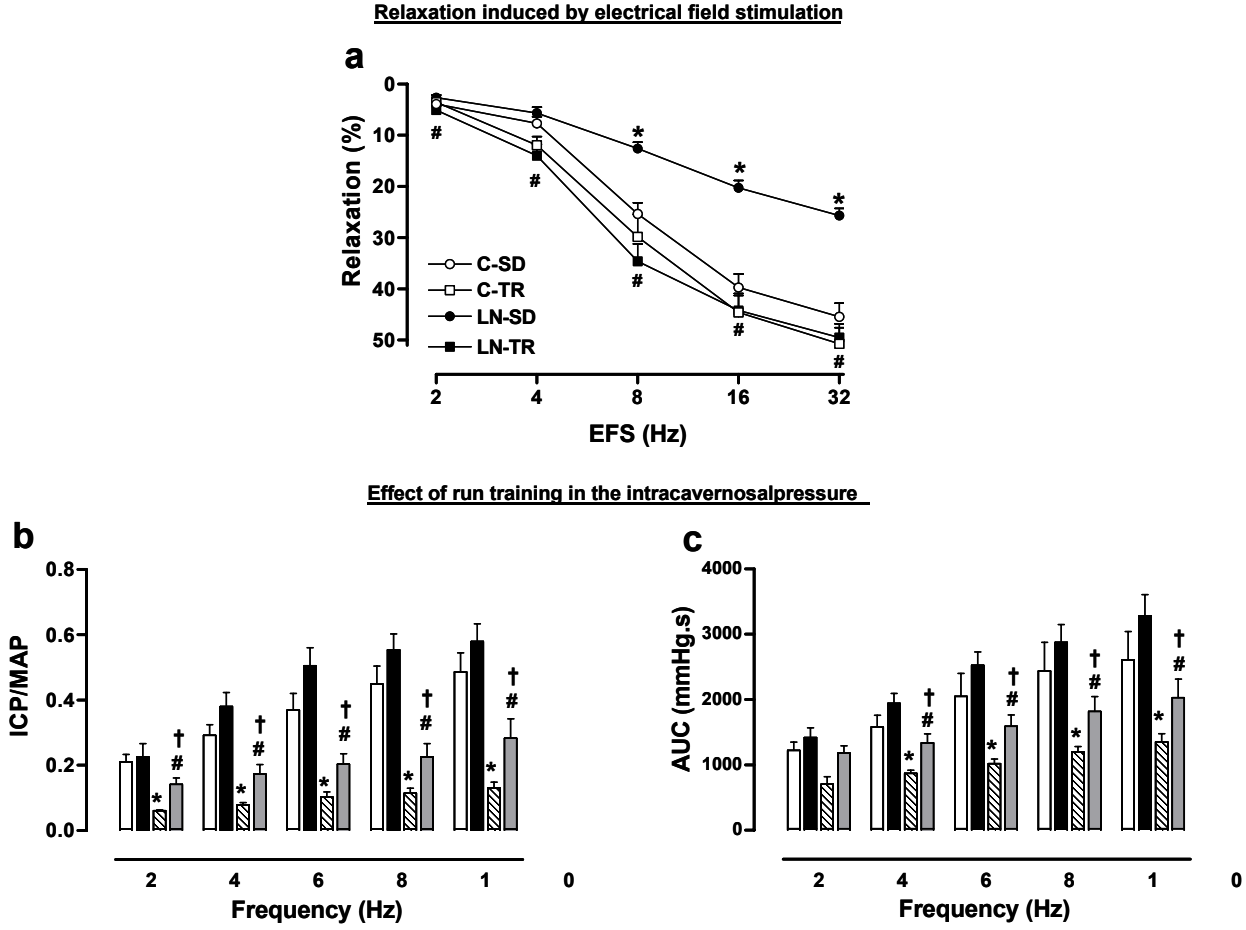

Figure 1
Effect of run training in EFS-induced relaxing response (2–32 Hz; *panel a*) and erectile function induced by electrical stimulation of cavernosal nerve (2–10 Hz; panel b and c). Erectile function is expressed as the ratio ICP/MAP and area under the curve (AUC).

± 2 μM). The run training program restored the NOx concentration in LN-TR group (26 ± 2 μM).

Experimental values were obtained from control sedentary (C-SD), control trained (C-TR), L-NAME sedentary (LN-SD) and L-NAME trained (LN-TR) animals. Data are mean ± S.E.M of 4–8 experiments. $^{*}P < 0.05$ compared to C-SD group; $^{\#}P < 0.05$ compared to LN-SD group; $^{\dagger}P < 0.05$ compared to C-TR.

Conclusion

Our findings show that run training significantly reverses the established erectile dysfunction due to impairment of the NO-GMPc signalling pathway in rats.

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